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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,241	01/17/2002	Bernhard Hauer	50531	6324

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/031,241	HAUER ET AL.	
	Examiner	Art Unit	
	YONG D. PAK	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,12,14-18 and 23-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,12,14-18 and 23-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 of PCT/EP00/07251.

Claims 11-12, 14-18, and 23-30 and are under consideration.

Election/Restrictions

Applicant's election with traverse of the species CYP102 in the reply filed on October 3, 2008 is acknowledged. The traversal is on the ground(s) that CYP4, CYP52, and CYP102 do share a special technical feature since they all contain cytochrome P450 as a functional group. This is not found persuasive because the technical feature linking CYP4, CYP52, and CYP102 appears to be that they all relate to cytochrome P450 enzyme. However, all three families of enzymes are known in the art. For example, Estabrook et al. (*Methods in Enzymology* – form PTO-1449) discloses a CYP102 cytochrome monooxygenase. Further, the claimed method of using a cytochrome P450 enzyme lacks an inventive step, as detailed below in the 103(a) rejection. Therefore, the technical feature linking the above species does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

Response to Arguments

Applicant's amendment and arguments filed on May 29, 2008, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14-15 recite specific amino acid residues of a cytochrome P450 monooxygenase. The metes and bounds of the phrase in the context of the claims are not clear. Without the recitation of a sequence identifier (i.e. SEQ ID NO), it is not clear to the Examiner as to which amino acids applicants are referring to.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 recites the phrase "the cytochrome P450 monooxygenase is a single mutant selected from the group consisting of F87A, F87V, L188K, V26T, R47F and V26T". The metes and bounds of this term in the context of the above claim are not

clear to the Examiner. It is not clear to the Examiner how a mutant P450 monooxygenase is a F87A, F87V, L188K, V26T, R47F and V26T. Examiner requests clarification of the above phrase.

Claim Rejections - 35 USC § 112- 1st paragraph

In view of applicant's argument, the rejection of claims 11-12 and 16-18 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, has been **withdrawn**.

In view of applicant's argument, the rejection of claims 11-12 and 16-18 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, has been **withdrawn**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11-12, 14, 16-18, and 23-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Estabrook et al. in view of Creaser et al., Voss et al. and Oliver et al.

Claim 11-12, 14, 16-18, and 23-30 drawn to a method for the enzymatic production of terminally or subterminally hydroxylated fatty acids comprising

hydroxylating fatty acids in the presence of an electro donor system, a cytochrome P450 monooxygenase or a mutant of a cytochrome P450 of SEQ ID NO:35 having a mutation at position 87, and oxygen, wherein said electron donor system is zinc dust/Co(III)sepulchrate.

Estabrook et al. (*Methods in Enzymology* – form PTO-1449) discloses a method for the enzymatic production of terminally or subterminally hydroxylated fatty acids comprising hydroxylating fatty acids in the presence of an electron donor system, a cytochrome P450 monooxygenase, oxygen, chloride ions and a hydrogen peroxide-cleaving enzyme, wherein said fatty acid is a C-12 fatty acid and wherein said electron donor system comprises a Co(III)sepulchrate mediator of Creaser et al.. Estabrook, et al. teaches that said mediator "retains chirality during reversible oxidation-reduction" (page 45, 1st paragraph).

The difference between the reference of Estabrook et al. and the instant invention is that the reference of Estabrook et al. does not teach a method of producing terminally or subterminally hydroxylated fatty acids using a Zn metal in powder form or a mutant of a cytochrome P450 of SEQ ID NO:35 having a mutation at position 87.

Creaser et al. (J. Am. Chem. Soc – form 1449) discloses a Zn/Co(III)sepulchrate electron donor system, which pioneered for the use of Co(III)sepulchrate as mediators in electrochemical reactions (Faulkner et al. – form PTO-1449, Reipa et al. – US Patent 6,126,795 and Roberts et al. – US Patent 6,492,132), wherein the Co(III)sepulchrate mediator is the same mediator used by Estabrook et al. Creaser et al. teaches that Zn dust causes reduction of the Co(III)sepulchrate mediator within seconds (page 3181).

Voss et al. (J Pharm Biomed Anal. 1999 Feb;19(1-2):127-33 - form PTO-892) discloses that enzymes undergo denaturation on metal electrodes during, eventually inactivating the enzyme (abstract).

Oliver et al. (Biochemistry 1997, 36, 1567-1572 – form PTO-892) discloses a mutant of SEQ ID NO:35 having a F87A mutation which hydroxylates fatty acids at the ω position, unlike the wildltype enzyme (abstract and page 1567).

Therefore, in combining the teachings of Estabrook et al., Creaser et al., Voss et al., and Oliver et al., it would have been obvious to one having ordinary skill in the art to modify the method of Estabrook et al. in hydroxylating fatty acids at the ω by using the mutant cytochrome P450 monooxygenase of Oliver et al. and using Zn dust as taught by Creaser et al. One of ordinary skill in the art would have been motivated to use the mutant cytochrome P450 monooxygenase of Oliver et al. because said mutant is able to catalyze ω hydroxylation of fatty acids. One of ordinary skill in the art would have been motivated to use Zn dust because Creaser et al. teaches that Zn dust causes immediate reduction, Zn dust is widely available (Sigma), and Voss et al. teaches that proteins denature on metal electrodes. One of ordinary skill in the art would have had a reasonable expectation of success since Estabrook et al. teaches a method of hydroxylating fatty acids with cytochrome P450 monooxygenases by replacing NADPH with an electrochemically generated reduction by the mediator Co(III)sepulchrate, Creaser et al. teaches a method of generating two electrons using the mediator Co(III)sepulchrate and Zn dust as the source of electrons, and Oliver et al. teaches a mutant that catalyzes ω hydroxylation of fatty acids.

Therefore, the above references render claims 11-12, 14, 16-18, and 23-30 *prima facie* obvious to one of ordinary skill in the art.

In response to the previous Office Action, applicants have traversed the above rejection. Applicants should note that the rejection has been amended.

Applicants argue that the claims are not obvious because there is no suggestion/guidance in Creaser et al. to use Zn dust in a biochemical system. Examiner respectfully disagrees. One of ordinary skill in the art would have been motivated to use Zn dust because Creaser et al. teaches that Zn dust causes immediate reduction, Zn dust is widely available (Sigma), and Voss et al. teaches that proteins denature on metal electrodes.

Applicants argue that there is no suggestion in Estabrook et al. to replace the metal electrode with a metal powder. The rejection has been amended. One of ordinary skill in the art would have been motivated to use Zn dust because Creaser et al. teaches that Zn dust causes immediate reduction, Zn dust is widely available (Sigma), and Voss et al. teaches that proteins denature on metal electrodes.

Applicants also argue that the claimed invention produces superior and unexpected results. Examiner respectfully disagrees. The instant rejection is not based on Estabrook et al. alone. The relative rates of the electron donor system for Estabrook et al. and Zn/Co(III)sepulchrate electron donor system is irrelevant because the rejection is based on the combined teachings of Estabrook et al., Creaser et al. and Voss et al. Further, Examiner notes that the claims do not recite any such limitations on the rate of reaction. Also, since Voss et al. teaches that proteins undergo denaturation

at metal electrodes, increased reaction using Zn dust/Co(III)sepulchrate electron donor system would not have been unexpected to one having ordinary skill in the art.

Hence the rejection is **maintained**.

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Yong D Pak/
Primary Examiner, Art Unit 1652